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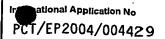
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR IDENTIFYING AN ANTI-STREPTOCOCCAL AGENT AND ITS USE FOR TREATING STREPTO-COCCAL INFECTIONS

(57) Abstract: A method for identifying an anti-streptococcal agent, comprises: (a) providing, as a first component, an isolated streptococcal M protein or a functional variant thereof; (b) providing, as a second component, isolated fibrinogen or a functional variant thereof; (b) providing, as a third component, an isolated β2 integrin or a functional variant thereof; (d) contacting said components with a test substance under conditions that would permit the components to interact in the absence of the test substance; and (e) determining whether the test substance inhibits the interaction between the components; thereby to determine whether a test substance is an anti-streptococcal agent.





A. CLASSIFICATION OF SUBJECT MATTER IPC 7 CO7K14/315 A61K39/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) I PC $\,\,7\,\,\,\,\,$ C $\,\,07K\,\,\,\,\,\,$ A $\,\,61K\,\,\,\,\,\,$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, Sequence Search

Category •	Citation of document, with indication, where appropriate, of the relevant passages	
	where appropriate, of the relevant passages	Relevant to claim No.
Y	CUE D. ET AL.: "A nonpeptide integrin antagonist can inhibit epithelial cell ingestion of Streptococcus pyogenes by blocking formation of integrin alpha5betal-fibronectin-M1 protein complexes." PROC. NATL. ACAD. SCI. USA, vol. 97, no. 6, 14 March 2000 (2000-03-14), pages 2858-2863, XP002306201	15—19, 22—26
	the whole document	1,11-14, 27,28

Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international	"T" later document published after the international filling date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention
document referring to an oral disclosure, use, exhibition or other means document published prior to the International filling date but later than the priority date claimed	cannot be considered to involve an inventive step when the document is combined with one or more other such document is combination being obvious to a person skilled in the art. *8* document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
12 January 2005	25/01/2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk	Authorized officer
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Giry, M

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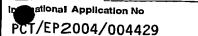
in pational Application No
PCT/EP2004/004429

C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/EP2004/004429
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DEMASTER E. ET AL.: "M+ group A	
	streptococci are phagocytized and killed in whole blood by C5a-activated polymorphonuclear leukocytes." INFECT. IMMUN	15,16
Υ	vol. 70, no. 1, January 2002 (2002-01), pages 350-359, XP002313110	
	abstract page 354, column 2 - page 356, column 1	1-14, 17-28
X	US 5 340 800 A (LIU D.Y. ET AL.) 23 August 1994 (1994-08-23) the whole document	15-19, 22-26
x	WO 03/014088 A (MERCK PATENT GMBH) 20 February 2003 (2003-02-20)	15,16
Y	claims 4-6,9	17,18, 22-24, 27,28
ĺ	page 6 page 31 — page 32	
Y	LEI B. ET AL.: "Evasion of human innate and acquired immunity by a bacterial homolog of CD11b that inhibits opsonophagocytosis." NATURE MEDICINE, vol. 7, no. 12, December 2001 (2001-12), pages 1298-1305, XP002243547 the whole document	1-28
r	RUF A. ET AL.: "Platelet-induced neutrophil activation: platelet-expressed fibrinogen induces the oxidative burst in neutrophils by an interaction with CD11c/CD18." BR. J. HAEMATOL., vol. 90, 1995, pages 791-796, XP009042496 cited in the application the whole document	1-28
,	SCHNITZLER N. ET AL.: "A co-stimulatory signal through ICAM-beta2 integrin-binding potentiates neutrophil phagocytosis." NATURE MEDICINE, vol. 5, no. 2, February 1999 (1999-02), pages 231-235, XP002313111 the whole document	1-28
,	WO 95/27736 A (INGELHEIM PHARMACEUTICALS, INC.) 19 October 1995 (1995-10-19) the whole document	1-28
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Form PCT/ISA/210 (continuation of second sheet) (January 2004)

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Α WO 00/34487 A (REGENTS OF THE UNIVERSITY 1-28 OF MINNESOTA) 15 June 2000 (2000-06-15) the whole document RASMUSSEN M. ET AL.: "Proteolysis and its Α 1-28 regulation at the surface of Streptococcus pyogenes." MOL. MICROBIOL., vol. 43, no. 3, 2002, pages 537-544, XP002313112 the whole document P,X HERWALD H. ET AL.: "M protein, a classical bacterial virulence determinant, 1-28 forms complexes with fibrinogen that induce vascular leakage." CELL, vol. 116, 6 February 2004 (2004-02-06), pages 367-379, XP002306203 the whole document

INTERNATIONAL SEARCH REPORT

ternational application No.

PCT/EP2004/004429

Box	No. I	Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)
1.	With r invent	regard to any nucleotide and/or amino acid sequence disclosed in the International application and necessary to the claimed tion, the international search was carried out on the basis of:
	a. 1	type of material X a sequence listing table(s) related to the sequence listing
	b. 1	format of material X in written format X in computer readable form
	c. t	x contained in the international application as filed x filed together with the international application in computer readable form furnished subsequently to this Authority for the purpose of search
2.		In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3.	Addition	onal comments:

INTERNATIONAL SEARCH REPORT

ternational application No. PCT/EP2004/004429

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 23-25, 28 because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 23-25 and 28 are directed to a method of treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/EP2004/004429

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
US 5340800	A	23-08-1994	AU AU CA EP JP WO	4048295 A 8631991 A 2090427 A1 0546077 A1 6500555 T 9203473 A1	04-04-1996 17-03-1992 28-02-1992 16-06-1993 20-01-1994 05-03-1992
WO 03014088	A	20-02-2003	DE WO	10139059 A1 03014088 A1	20-02-2003 20-02-2003
WO 9527736	Α	19-10-1995	CA EP JP WO	2187360 A1 0757697 A1 9512252 T 9527736 A1	19-10-1995 12-02-1997 09-12-1997 19-10-1995
WO 0034487	A	15-06-2000	US BR CA CN EP JP WO US	6355255 B1 9915988 A 2354508 A1 1329669 T 1137785 A1 2002531584 T 0034487 A1 2002142009 A1 2004062777 A1	12-03-2002 04-09-2001 15-06-2000 02-01-2002 04-10-2001 24-09-2002 15-06-2000 03-10-2002 01-04-2004

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